Surgical management of early stage invasive breast cancer: a practice guideline

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Objectives: To assess the available evidence on sentinel lymph-node biopsy, and to examine the long-term follow-up data from large randomized phase III trials comparing breast-conserving therapy with mastectomy in order to make recommendations on the surgical management of early invasive breast cancer (stages I and II), including the optimum management of the axillary nodes: for the breast — modified radical mastectomy or breast-conserving therapy; for the axilla — complete axillary node dissection, axillary dissection of levels I and II lymph nodes, sentinel lymph-node biopsy or no axillary node surgery. **Outcomes:** Overall survival, disease-free survival, local recurrence, distant recurrence and quality of life. **Evidence:** MEDLINE, EMBASE, the Cochrane Library databases and relevant conference proceedings were searched to identify randomized trials and meta-analyses. Two members of the Practice Guidelines Initiative, Breast Cancer Disease Site Group (BCDSG) selected and reviewed studies that met the inclusion criteria. The systematic literature review was combined with a consensus process for interpretation of the evidence to develop evidence-based recommendations. This practice guideline has been reviewed and approved by the BCDSG, comprising surgeons, medical oncologists, radiation oncologists, pathologists, a medical sociologist, a nurse representative and a community representative. **Benefits, harms and costs:** Breast-conserving therapy (lumpectomy with levels I and II axillary node dissection, plus radiotherapy) provides comparable overall and disease-free survival to modified radical mastectomy. Levels I and II axillary dissection accurately stages the axilla and minimizes the morbidity of axillary recurrence but is associated with lymphedema in approximately 20% of patients and arm pain in approximately 33%. Currently, there is insufficient data regarding locoregional recurrence and long-term morbidity associated with sentinel-node biopsy to advocate it as the standard of care. Breast-conserving therapy may offer an advantage over mastectomy in terms of body image, psychological and social adjustment but appears equivalent with regard to marital adjustment, global adjustment and fear of recurrence. **Recommendations:** Women who are eligible for breast-conserving surgery should be offered the choice of either breast-conserving therapy with axillary dissection or modified radical mastectomy. Removal and pathological examination of levels I and II axillary lymph nodes should be the standard practice in most cases of stages I and II breast carcinoma. There is promising but limited evidence to support recommendations regarding sentinel lymph-node biopsy alone. Patients should be encouraged to participate in clinical trials investigating this procedure. **Validation:** A draft version of this practice guideline and a 21-item feedback questionnaire was circulated to 201 practitioners in Ontario. Of the 131 practitioners who returned the questionnaire, 98 (75%) completed the survey and indicated that the report was relevant to their clinical practice. Eighty (82%) of these practitioners agreed that the draft document should be approved as a practice guideline. **Sponsors:** The Practice Guidelines Initiative is supported by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care. **Completion date:** Jan. 21, 2003.

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Objectifs : Évaluer les données probantes disponibles sur la biopsie du ganglion lymphatique sentinelle et examiner les données de suivi à long terme provenant de grandes études cliniques randomisées de phase III, dans lesquelles le traitement de conservation du sein est comparé avec la mastectomie, en vue de formuler des recommandations sur la prise en charge chirurgicale d'un cancer du sein envahissant à un stade précoce (stades I et II), y compris la prise en charge optimale des ganglions axillaires : au niveau du sein — la mastectomie radicale modifiée ou la chirurgie mammaire conservatrice; dans la région axillaire — l'exérèse totale des ganglions lymphatiques, l'évidement axillaire des ganglions lymphatiques de niveaux I et II, la biopsie du ganglion lymphatique sentinelle, ou aucune chirurgie ciblant les ganglions lymphatiques. **Résultats :** La survie, la survie sans récidive, la récidive locale, la récidive à distance et la qualité de vie. **Données probantes :** On a effectué des recherches dans les bases de données MEDLINE, EMBASE et Cochrane Library, ainsi que dans des actes de conférences pertinentes, pour trouver des études cliniques randomisées ainsi que des méta-analyses. Deux membres du Groupe de travail sur les sites du cancer du sein (GTSCS) de l'Initiative sur les lignes directrices de pratique ont choisi et passé en revue les études qui satisfaisaient aux critères d'inclusion. On a combiné un examen systématique des documents avec un exercice de concertation portant sur l'interprétation des données probantes afin de formuler des recommandations factuelles. Le GTSCS, constitué de chirurgiens, de médecins oncologues, de radio-oncologues, de pathologistes, d'un sociologue médical, d'une représentante des infirmières et d'un représentant communautaire, a étudié et approuvé ce guide de pratique. **Avantages, préjudices et coûts :** Par rapport à la mastectomie radicale modifiée, le traitement de conservation du sein (tumorectomie avec évidement des ganglions lymphatiques de niveaux I et II conjuguée avec une radiothérapie) offre des résultats comparables sur le plan de la survie et de la survie sans récidive. L'évidement axillaire de niveaux I et II permet d'établir avec exactitude le niveau d'atteinte dans le creux axillaire et de réduire au minimum la morbidité associée à la récidive dans cette région. Cette intervention est néanmoins associée au lymphœdème, qui touche environ 20 % des patientes, ainsi qu'à de la douleur au bras, qui touche environ 33 % d'entre elles. À l'heure actuelle, il n'y a pas suffisamment de données probantes au sujet des récidives loco-régionales et de la morbidité à long terme associées à la biopsie du ganglion lymphatique sentinelle pour qu'on recommande cette intervention comme norme de soin. La chirurgie mammaire conservatrice pourrait être plus avantageuse que la mastectomie sur le plan de l'image corporelle et de l'adaptation psychologique et sociale, mais les deux interventions semblent équivalentes en ce qui concerne l'adaptation dans le couple, l'adaptation globale et la peur de la récidive. **Recommandations :** On devrait offrir aux femmes qui sont de bonnes candidates pour la chirurgie mammaire conservatrice le choix de subir soit le traitement de conservation du sein conjugué avec un évidement axillaire, soit une mastectomie radicale modifiée. Il faudrait que l'ablation et l'examen pathologique des ganglions lymphatiques axillaires de niveaux I et II constituent la pratique privilégiée dans la plupart des cas de cancer du sein de stades I et II. Des données probantes prometteuses, quoique limitées, appuient les recommandations au sujet de la seule biopsie du ganglion lymphatique sentinelle. Il faudrait encourager les patientes à participer à des études cliniques portant sur cette intervention. **Validation :** On a fait parvenir une version provisoire de ce guide de pratique ainsi qu'un questionnaire de rétroaction comptant 21 questions à 201 praticiens en Ontario. Au nombre des 131 praticiens qui ont renvoyé le questionnaire, 98 (75 %) avaient répondu aux questions et indiquaient que le rapport était pertinent dans leur pratique. Quatre-vingt (82 %) des praticiens estimaient qu'il faudrait approuver le document provisoire comme guide de pratique. **Commanditaires :** Action Cancer Ontario et le ministère de la Santé et des Soins de longue durée de l'Ontario appuient l'Initiative sur les lignes directrices de pratique. **Complété :** 21 janvier 2003.

Breast cancer is the most commonly diagnosed cancer among Canadian women, excluding nonmelanoma skin cancer. In 2004, this disease will have been diagnosed in an estimated 21 200 women in Canada.[1] The majority of these women will have operable breast cancer.

Surgery continues to play a prominent role in the management of early invasive breast cancer. Over the last 2 decades, breast-conserving therapy has become established as a viable alternative to modified radical mastectomy. More recently, sentinel lymph-node biopsy has shown promise as a conservative approach to staging the axilla. At present, axillary dissection of levels I and II lymph nodes is standard in Canada. This procedure accurately stages the axilla and minimizes the risk of axillary recurrence. However, in some women, axillary dissection is associated with infection, cutaneous numbness and dysesthesia, and significant lymphedema.[2] A less invasive method of axillary evaluation is very appealing given the potential morbidity associated with axillary dissection. However, caution is warranted before adopting a more conservative staging procedure. Axillary lymph-node status remains the single most important prognostic factor for breast cancer.[3] Adjuvant systemic and regional therapy decisions are based, in large part, on whether, and to what extent, axillary lymph nodes are involved.

A practice guideline for the surgical management of early stage invasive breast cancer was originally completed in 1996 and subsequently

published.[4] The rationale for revisiting the practice in this evidence-based practice guideline is 2-fold: (1) to assess the available evidence on sentinel-node biopsy, and (2) to examine the long-term follow-up data from the large randomized phase III trials comparing breast-conserving therapy to mastectomy.

Methods

Literature search strategy

We searched MEDLINE (1966–April 2004), EMBASE (1980–April 2004) and the Cochrane Library (issue 1, 2004). The strategy used disease-specific terms (breast neoplasms/ or breast cancer [tw] or mammary neoplasms/) in combination with treatment-specific terms (mastectomy/ or mastectomy [tw, sh] or mastectomy or segmental/ or lumpectomy [tw] or breast conserv [tw] or conserv [tw] or sentinel [tw] or axilla [tw]) and terms specifically for study design and publication type (meta-analysis [pt, sh, tw] or randomized controlled trial [sh, pt, tw] or randomized controlled trials/ or random [tw]). The search was not limited by language of publication.

The Physician Data Query (PDQ) clinical trials database on the Internet (www.cancer.gov/search/clinical_trials/) and the proceedings of the annual meetings (1999–2003) of the American Society of Clinical Oncology and the American Society for Therapeutic Radiology and Oncology were searched for reports of new trials. Relevant studies were retrieved and reviewed by 2 Breast Cancer Disease Site Group (BCDSG) members. References lists of included studies were searched for additional trials.

Inclusion criteria

Published abstracts and full reports were eligible for inclusion if they were randomized controlled trials (RCTs) or meta-analyses comparing (a) breast-conserving therapy to mastectomy or (b) the surgical management of the axilla by either complete axillary node clearance, dissection of levels I and II lymph nodes, sentinel-node biopsy or no axillary surgery. Randomized trials or meta-analyses investigating the efficacy and safety of sentinel-node biopsy were also eligible. Outcomes of interest included overall or disease-free survival, local recurrence, distant recurrence and quality of life.

Synthesizing the evidence

A quantitative synthesis of the data from randomized trials comparing breast-conserving surgery and mastectomy was not undertaken for this practice guideline, as 3 meta-analyses have been conducted and published on this topic.[5–7] Similarly, it was decided not to pool the results of randomized trials comparing mastectomy or lumpectomy plus radiation with or without axillary dissection because a published meta-analysis was available[8] that synthesized the data from all of the randomized trials identified on this topic.

Guideline development

This practice guideline report was developed by the Practice Guidelines Initiative of Cancer Care Ontario's Program in Evidence-Based Care, using the methodology of the Practice Guidelines Development Cycle.[9] Evidence was selected and reviewed by members of the Practice Guidelines Initiative's BCDSG and methodologists.

The guideline is a convenient and up-to-date source of the best available evidence on the surgical management of early stage breast cancer, developed through systematic reviews, evidence synthesis and input from practitioners in Ontario. The body of evidence in this report primarily comprises RCT data; therefore, recommendations by the BCDSG are offered. The report is intended to enable evidence-based practice. The Practice Guidelines Initiative is editorially independent of Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

External review by Ontario practitioners was obtained through a mailed survey consisting of items that address the quality of the draft practice guideline report and its recommendations and whether the recommendations should serve as a practice guideline. Final approval of the original guideline report has been obtained from the Practice Guidelines Coordinating Committee.

The Practice Guidelines Initiative has a formal standardized process to ensure the currency of each guideline report. This consists of the periodic review and evaluation of the scientific literature and, where appropriate, integration of the literature with the original guideline information. This document replaces the practice guideline report on the surgical management of early stage breast cancer originally completed in 1996.[4] The recommendation concerning breast-conserving therapy versus mastectomy is similar to that made in 1996, but new recommendations on axillary lymph-node dissection and sentinel-node biopsy have been added.

Results

Literature search results

We identified 10 RCTs and 2 unpublished studies (see Table 1[10–19]) and 3 meta-analyses[5–7] that compared the effect of breast-conserving therapy to mastectomy on overall survival or recurrence. Surgical management of the axilla was evaluated in 6 RCTs[17,18,20–28] and 1 meta-analysis[8] on axillary dissection. One RCT[29] and 1 meta-analysis[30] of case series on sentinel-node biopsy were found. The literature search also identified 14 papers that reported quality-of-life data from randomized trials of breast-conserving therapy versus mastectomy[31–44] and 1 meta-analysis[45] on the topic.

Surgical management: breast-conserving therapy versus mastectomy

Key results from the 12 randomized trials that compare breast-conserving therapy with mastectomy for women with early stage breast cancer are summarized in Table 1 (unpublished data).[10–19] Six trials are considered the standard in the field.[10–15] Of the remaining 6 trials, the Argentinean[16] and the 2 Guy's Hospital series[17,18] had significant methodologic irregularities, and results from 3 trials reported in the meta-analysis by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG)[5] were never published (2 trials) or only published in abstract form[19] (1 trial).

With the exception of the 2 Guy's Hospital trials,[17,18] no significant differences were reported in overall survival, disease-free survival or distant disease-free survival in any of the studies comparing breast-conserving surgery and mastectomy.

All 3 published meta-analyses of RCTs comparing mastectomy and breast-conserving surgery reported no significant difference in survival between the 2 groups.[5–7] (The Argentinean[16] and Guy's Hospital series[17,18] were not included in these analyses.) The EBCTCG study included data from 4891 women who participated in 9 RCTs of mastectomy versus breast-conserving surgery plus radiotherapy.[5] They reported a nonsignificant odds reduction for death of –2% (standard error, 7), which represented a 2% increase in the odds of death in the mastectomy group compared with the breast-conserving therapy group ($p = 0.7$).

In 1997, Morris and colleagues[6] published a meta-analysis using a combination of individual patient data and published results from 6 randomized trials. They reported pooled odds ratios for death of 0.90 (95% confidence interval [CI] 0.74–1.09) at 5 years after randomization and 0.91 (95% CI 0.78–1.05) at 10 years. In 1998, abstract data from another meta-analysis by Morris and associates[7] reported long-term data from 3 RCTs. After up to 20 years' follow-up, no significant differences were detected between pooled overall survival (55% v. 48%, log rank $p = 0.95$) or distant recurrence (38% v. 36%, log rank $p = 0.61$) in the mastectomy and the breast-conserving therapy arms respectively.

Table 1

Randomized trials comparing breast-conserving therapy with mastectomy

Study	Comparison*	No. of patients	Time point, yr	Overall survival, %	Disease-free survival, %	Local recurrence, %†
Fisher et al[10]	Lumpectomy	634		53	64	39‡
	Lumpectomy and radiation	628	20	50	62	14
	Total mastectomy	589		51	63	—
Veronesi et al[11]	Quadrantectomy and radiation	352	20	41	NR	8‡
	Modified radical mastectomy	349		42	NR	2
van Dongen et al[12]	Breast-conserving surgery	448	10	65	47	20‡
	Modified radical mastectomy	420		66	53	12
Arriagada et al[13]	Tumorectomy and radiation	88	22	60	NR	9
	Modified radical mastectomy	91		49	NR	14
Poggi et al[14]	Lumpectomy and radiation	121	18	54	63	NR
	Modified radical mastectomy	116		58	67	NR
Blichert-Toft et al[15]	Breast-conserving surgery	430	6	79	70	2
	Total mastectomy	429		82	66	—
Gori et al[16]	Tumorectomy	58	5	95	NR	8
	Madden's procedure	63		93	NR	2
Hayward[17]	Wide excision and radiation	122	6	NR	NR	30‡
	Total mastectomy and radiation	130				8
Atkins et al[18]	Wide excision and radiation	184	10	NR	NR	40‡
	Total mastectomy and radiation	192				18
D'Aiuto et al[19]	Breast-conserving surgery	170	NR	88	NR	NR
	Mastectomy	170		85		
CRC UK, 1995§	Breast-conserving surgery	71	NR	80	NR	NR
	Mastectomy	74		82		
BMFT 01 Germany, 1995§	Breast-conserving surgery	41	NR	90	NR	NR
	Mastectomy	31		95		

*Axillary dissection was carried out in all patients except for the breast conservation arms in the 2 Guy's Hospital trials.[17,18]
†There was substantial variability between studies in how local or locoregional recurrence was defined.
‡Indicates a significant difference at $p < 0.05$.
§The results of these studies are published in abstract form only.
BMFT = Bundesministerium für Forschung und Technologie; CRC UK = Cancer Research Campaign United Kingdom.

Axillary node dissection

Results from 6 randomized trials of axillary node dissection versus no axillary node dissection[17,18,20–28] were summarized in the meta-analysis by Orr.[8] This meta-analysis was based on 4 decades of data from 2936 women who participated in 6 randomized trials comparing mastectomy or lumpectomy plus radiation with or without axillary dissection. Trials were eligible for inclusion if they included patient populations with stage I or a combination of stages I and II disease. In 2 trials, the mean tumour size was not reported; 3 trials reported average tumour sizes greater than 3 cm, with positive nodes in 39%–54% of women. The authors of the meta-analysis reported that it was unlikely that any of the women had mammographically detected tumours and that adjuvant treatment with chemotherapy or tamoxifen would rarely have been used at the time these trials were conducted. The 6 trials reported an absolute survival benefit with axillary dissection ranging from 4% to 16%, which corresponds to a 7%–46% relative reduction in the risk of death. Orr reported a significant pooled survival benefit of 5.4% (95% CI 2.7%–8.0%, $p < 0.01$) favouring axillary dissection. However, the results must be viewed with caution since this meta-analysis was based only on published data rather than on individual patient data. Also, procedures other than levels I and II axillary node dissection were used in some of the studies, and in others axillary radiation was given to those who did not undergo axillary surgery. Although this meta-analysis suggests a significant survival benefit with axillary dissection, evolving approaches in surgical management, radiotherapy, adjuvant systemic therapy and screening practices may limit the magnitude of the survival benefit on women treated with current breast cancer therapy.

Longer term results for 2[20,28] of the 6 trials were identified.[46,47] In the study from the Institut Curie, overall survival had decreased from 97% and 93% ($p = 0.014$) at 4.5 years to 76% and 74% (p = NS) at 15 years in the axillary dissection group versus the axillary radiotherapy group.[47] The lack of difference in disease-free survival, metastases and local recurrence was maintained. Recurrences in axillary nodes were still less frequent in the axillary dissection group (1% v. 3%, $p = 0.04$). In the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-04 study, 25-year follow-up failed to show a significant difference in overall survival between the groups with and without axillary dissection (25% v. 26% respectively).[46] Rates of distant disease-free survival were 46% and 43% in the groups with and without axillary dissection respectively (HR = 1.10, 95% CI 0.89–1.35). These results tend to diminish the conclusions from the meta-analysis.

Sentinel lymph-node biopsy versus axillary dissection

To date, only 1 RCT has published data comparing sentinel-node biopsy with axillary node dissection.[29] In this trial from Milan, 516 women who had undergone quadrantectomy and sentinel-node biopsy were randomized to axillary node dissection or axillary node dissection only if the sentinel node contained metastatic cancer (SNB group). At a median follow-up of 46 months, there were 15 breast cancer events (ipsilateral or contralateral breast cancer or regional nodal or distant metastases) in the axillary node dissection group compared with 10 in the SNB group ($p = 0.26$). Two women died of breast cancer in the axillary node dissection group compared with 1 in the SNB group ($p = 0.26$).

One large ongoing randomized trial is comparing sentinel-node biopsy and axillary dissection. Similar to the Milan trial, the NSABP B-32 trial will evaluate sentinel-node biopsy with or without axillary node dissection.[48] Furthermore, a number of ongoing trials are studying women with positive sentinel nodes. The American College of Surgeons Oncology Group (ACOSOG) Z0010 trial is a prognostic study of sentinel-node and bone marrow micrometastases in women with early breast cancer.[49] The ACOSOG Z0011 trial will evaluate the effectiveness of axillary node dissection in women who have a positive sentinel node.[50] The International Breast Cancer Study Group (IBCSG) 23-01 trial will also compare the effectiveness of axillary node dissection in women with sentinel-node-positive disease.[51] The European Organization for the Research and Treatment of Cancer (EORTC) 10981 trial will compare axillary node dissection with axillary radiotherapy in sentinel-node-positive women.[52] Of note, only the ACOSOG Z0011, the IBCSG 23-01, and the EORTC 10981 trials were still recruiting patients as of May 2004.

In 1999, Miltenburg and colleagues[30] published a meta-analysis of 11 case series in the literature between 1993 and 1998. Data were reported for 912 women with breast cancer who had sentinel-node biopsy followed by axillary node dissection. Overall, sentinel lymph nodes were successfully identified in 84% of women and concordance with pathological results from axillary dissection was confirmed in 98% of women. There was a 5% false-negative rate associated with sentinel-node biopsy. The highest identification rates were reached using either radiocolloid or dye and radiocolloid combined. In fact, between January 1991 and December 2000, over 50 studies (involving more than 9000 women) have been reported.[53] The studies were all case series, some prospective and some retrospective. In all of these studies, patients first had a sentinel-node biopsy, followed by an axillary dissection. The false-negative rate ranged from 0% to

22%. It is important to note that falsely staging the presence of nodal metastases may affect the treatment a patient receives after surgery and possibly the chances of breast cancer recurrence.

Quality of life for women who choose breast-conserving therapy over mastectomy

Fourteen papers on quality of life, using data from randomized trials of breast-conserving surgery versus mastectomy, have been published.[31–44]

Poulsen and colleagues[31] reported on 184 women who participated in the Danish Breast Cancer Cooperative Group trial. Over an average follow-up of 31 months, no significant differences were found between the 2 types of surgery on measures of physical state, emotional state, social activity, work activity, body image, marital and sexual life or level of anxiety.

Curran and associates[32] analyzed data from 278 women who participated in the European Organization for the Treatment of Cancer trial. Two years postoperatively, women in the breast-conserving therapy group had better body image ($p = 0.001$) and were more satisfied with treatment ($p = 0.001$) than those in the mastectomy group; there was no significant difference between the 2 groups with respect to fear of cancer recurrence ($p = 0.236$).

Although survival results are not yet forthcoming, quality-of-life data from the EORTC 10850 trial have been published.[44] In 136 women aged 70 years and older, women who underwent breast-conserving and tamoxifen therapy did not differ from those receiving mastectomy in terms of treatment preference, fatigue, emotional function, fear of recurrence, social support, physical functioning and leisure-time activities. Women who underwent breast-conserving therapy did, however, report fewer arm problems ($p = 0.04$) and a trend toward improved body image ($p = 0.06$).

Data from the remaining 11 randomized trials[33–43] form the basis of the meta-analysis by Moyer.[45] Results favouring breast-conserving therapy were reported in 10 trials for psychological adjustment (mean weighted effect size [MWES] = 0.060, standard deviation [SD] 0.66, $p < 0.001$) and in 3 trials for social adjustment (MWES = 0.334, SD 0.140, $p < 0.05$). No significant differences were detected in 7 trials measuring marital and sexual adjustment ($p > 0.05$) or body self image ($p > 0.05$), or in 6 trials measuring cancer-related fears and concerns ($p > 0.05$). The pooled effect size for global adjustment from 3 studies favoured mastectomy but was not statistically significant (MWES = –0.20, SD 0.108, $p > 0.05$).

Preoperative chemotherapy

Preoperative chemotherapy has been compared to the same chemotherapy given postoperatively in a number of randomized trials.[54–56] None have shown any difference in disease-free or overall survival, but all have shown an increased likelihood of breast-conserving surgery in the preoperative chemotherapy arms. A study conducted at the Royal Marsden Hospital, London, using mitoxantrone and methotrexate chemotherapy, detected an 87% breast-conserving surgery rate in the preoperative chemotherapy arm compared with 72% in the postoperative arm ($p < 0.005$).[54] In the NSABP B-18 trial using doxorubicin and cyclophosphamide chemotherapy, 68% versus 60% of patients had breast-conserving surgery in favour of the preoperative treatment (p value not reported).[55] The EORTC study used fluorouracil, epirubicin and cyclophosphamide preoperatively versus postoperatively. In the preoperative group, 23% of the women who were considered initially to require mastectomy had breast-conserving surgery after preoperative chemotherapy.[56] The European Cooperative Trial in operable breast cancer used doxorubicin and paclitaxel for 4 cycles followed by 4 cycles of cyclophosphamide, methotrexate and fluorouracil, either pre- or postoperatively.[57] The primary tumour had to be more than 2 cm in dimension. Breast-conserving surgery rates were 71% in the preoperative group versus 35% in the postoperative group ($p < 0.0001$).

Practitioner feedback results

In October 2001, 201 practitioners (42 medical oncologists, 41 radiation oncologists and 118 surgeons) were surveyed. Of the 131 practitioners who returned the questionnaire, 98 (75%) completed the survey and indicated that the report was relevant to their clinical practice; 89 (91%) of them indicated that they would use the draft recommendations in their practice, and 80 (82%) agreed that the draft guideline should be approved as a practice guideline. Twenty-six respondents provided written comments. There was mixed feedback on the role of sentinel-node biopsy outside clinical trials. Some practitioners urged the adoption of sentinel-node biopsy by adequately trained surgeons. Others wanted clear evidence of survival equivalence before adopting sentinel-node biopsy as standard practice. Some practitioners questioned the need for axillary node dissection in elderly women with receptor-positive cancers who would be receiving tamoxifen regardless of the results of the dissection.

In response to the practitioner feedback survey, minor changes were made to the guideline report but not to the recommendations. The rationale for full dissection when the sentinel lymph node is positive for metastatic disease was added to the guideline report. The issue of sentinel-node biopsy alone, outside a clinical trial, was discussed by the committee, as well as the reference by a number of respondents to the Canadian practice guideline on sentinel lymph-node biopsy by the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Can-

cer.[2] The Canadian guideline recommends that axillary node dissection remain the standard of care and that, if a patient requests or is offered sentinel-node biopsy alone, she needs to be made aware of the risks and benefits and what is and what is not yet known about the procedure. The Canadian guideline confirms the lack of data from randomized trials comparing outcomes from sentinel-node biopsy to those with axillary node dissection; therefore, participation in randomized trials is encouraged. Since there is little evidence from randomized trials, the Canadian guideline is based on a consensus of the Steering Committee. In the opinion of the BCDSG although this consensus statement was reasonable, sentinel-node biopsy alone could not be recommended in the absence of high-quality evidence at the time of writing. No change was made to the guideline.

With regard to the omission of axillary node dissection in elderly hormone-receptor-positive women receiving tamoxifen, it is recognized that there may be some cases in which the omission of axillary node dissection could be justified. However, there are no randomized data confirming that such women do as well without as with axillary node dissection, and so omission of axillary node dissection cannot be recommended as standard care. The International Breast Cancer Study Group is currently conducting a randomized trial comparing complete axillary dissection to tamoxifen in elderly women, and the group's study addresses this question.[58]

Discussion

For eligible candidates, surgical treatment options for early stage invasive breast carcinoma include breast-conserving surgery plus radiation or mastectomy. Six fully published RCTs[10–15] have demonstrated comparable results between standard breast-conserving therapy and mastectomy in terms of overall survival and disease-free survival.

Although evidence relating quality of life to the extent of breast surgery is conflicting, women should be fully informed of the treatment implications involved with both mastectomy and breast-conserving surgery (i.e., the potential need for additional surgery and for adjuvant radiation therapy following breast-conserving surgery).

Evaluation of axillary lymph-node disease is an integral part of adjuvant treatment planning for most patients with stages I and II breast cancer. Although the surgical treatment of the axilla in cases of early stage breast cancer may or may not contribute significantly to a reduction in mortality in today's patient populations, it reduces the morbidity of axillary recurrence.

Axillary lymph-node dissection is the current standard of surgical care. It carries significant risk of lymphedema and long-term postoperative dysthesias. With no set criteria used to define lymphedema and a variety of assessment techniques in use, there is wide variation in reported rates of lymphedema following axillary dissection. Rates ranging from 2% to 70% have been reported.[59] In a recent study, arm morbidity was assessed in 110 women after partial mastectomy with axillary dissection and in most cases, irradiation.[60] Lymphedema (defined as a >10% increase in arm volume) developed in 19% of the women, and 49% had reduced arm mobility (defined as a 15° impairment of shoulder mobility). After 5 years, 31% of women continued to report some arm pain after breast-conserving therapy.

However promising, investigations for axillary staging such as sentinel-node biopsy have not yet demonstrated acceptable specificity and sensitivity to be used routinely outside the context of a clinical trial. Although sentinel-node biopsy alone is currently not a standard practice, a position paper by McCready and colleagues[61] recommends that surgeons consider acquiring the necessary equipment, training and infrastructure to perform this technique. Surgeons should also collaborate with their colleagues in pathology and nuclear medicine to develop techniques and standards for proper handling and pathological assessment of these nodes.

Breast Cancer Disease Site Group consensus

With no observed differences in overall survival or distant recurrence, the opinion of the BCDSG was that, for eligible candidates, the choice between breast-conserving therapy and modified radical mastectomy should be based on patient preference.

To make an informed decision, patients should be fully aware of the risks and benefits of each procedure. Breast-conserving therapy typically involves tumour excision with uninvolved margins, axillary dissection and adjuvant breast irradiation. There is also a potential need for further surgery, possibly a mastectomy, in cases of local recurrence. A modified radical mastectomy involves the removal of the entire breast, including the nipple and areola complex, and the fascia over the pectoralis muscles, while sparing the underlying muscles and innervation. Breast reconstruction is an option for women who choose mastectomy.

The DSG agreed that at present there is insufficient evidence to make recommendations regarding sentinel-node biopsy alone. The group acknowledged that some clinicians in Ontario are beginning to train for the procedure and are building expert teams in anticipation of the potential demand should sentinel-node biopsy alone become standard practice. The BCDSG agreed that patients should be encouraged to participate in clinical trials investigating this procedure.

Given that quality-of-life measures are difficult to capture objectively, the BCDSG believed that the evidence surrounding quality of life af-

ter surgery was conflicting. Whereas some evidence suggests that women who undergo breast-conserving therapy may have higher body self image than those who undergo mastectomy, other measures of psychosocial well-being were inconclusive.

Preoperative chemotherapy in patients with operable breast cancer does not appear to improve disease-free or overall survival, but it does increase the likelihood of breast-conserving surgery. The BCDSG therefore felt that preoperative chemotherapy could be considered for those who desire breast-conserving surgery but are not believed initially to be a good candidate because of the size of the tumour in relation to the size of the breast.

Practice guideline

This practice guideline applies to women with early stage (stages I and II) invasive breast cancer who are eligible for either breast-conserving therapy or mastectomy.

Recommendations

- Women who are eligible for breast-conserving therapy should be offered the choice of either breast-conserving therapy with axillary dissection or modified radical mastectomy.
- Removal and pathological examination of levels l and II axillary lymph nodes should be the standard practice in most cases of stages I and II breast carcinoma.
- Because, there is promising but limited evidence, not yet sufficient, to support a recommendation for sentinel lymph-node biopsy alone, patients should be encouraged to participate in clinical trials investigating this procedure.

Qualifying statements

- With no difference in survival or distant recurrence, the choice between breast-conserving therapy with axillary dissection and modified radical mastectomy should depend on patient preference when appropriate.
- Each patient should be fully informed of the risks and benefits of each procedure.
- Patients should be aware that breast-conserving therapy involves tumour excision with uninvolved margins, axillary dissection and adjuvant breast irradiation.
- Patients who choose breast-conserving therapy should be aware that there is the potential need for further surgery, possibly a mastectomy, in cases of local recurrence.
- Evidence surrounding quality of life after surgery is conflicting, but there is some evidence suggesting that women who receive breast-conserving therapy may have higher body self image than those who undergo mastectomy.
- In some instances, preoperative chemotherapy can shrink a larger primary tumour and allow for breast-conserving surgery followed by breast irradiation rather than mastectomy.

Practice guideline date

Jan. 21, 2003. Practice guidelines developed by the Practice Guidelines Initiative are reviewed and updated regularly. Please visit the Practice Guidelines Initiative Program in Evidence-Based Care section of the Cancer Care Ontario Web site (www.cancercare.on.ca) for updates to this guideline.

Addendum

Since completion of this practice guideline and submission of this article, the North American clinical trials designed to assess sentinel-node biopsy have closed for accrual. Despite the lack of any new high-quality evidence, sentinel-node biopsy has become the routine method used to assess axillary nodal status for early stage breast cancer in many centres.

Competing interests: None declared.

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Correction

In a case report in the April 2005 issue of the journal (*Can J Surg* 2005;48[2]:159-60), one of the authors' names was misspelled. The author byline on page 159 should read as follows: Shahzeer Karmali, MD, BSc;* Luke Rudmik, MD;* Walley Temple, MD;* Vincent Falck, MB ChB;† Gregory McKinnon, MD*